

Stem cell tourism and Canadian family physicians

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The provision of unproven stem cell-based treatments by clinics in countries around the world—a phenomenon that has been called *stem cell tourism*—is a growing trend with implications for both the practice of family medicine and the health and safety of the Canadian public.^{1*} Canadians place trust in their family physicians, who have a central role in continuity of care. This empowers Canadian family physicians to address many of the social and clinical challenges created by stem cell tourism. When individuals interested in pursuing these treatments consult their family physicians, an invaluable opportunity is presented to provide information about the treatments' very real potential harms and limitations. This exchange is necessary for physicians seeking to act in the best interests of their patients and to support patient autonomy in decision making, particularly in light of the poor quality of information made available by many of the clinics offering such treatments. Discussion of relevant considerations in assessing unproven therapies is particularly important when children or other individuals without decision-making capacity are involved. These groups are particularly vulnerable, and children appear to account for a meaningful proportion of the individuals receiving these treatments.²

Few areas of biomedical inquiry hold as much potential as stem cell research. If research in this area progresses as hoped, cell-based therapies for a range of disorders might one day become available. However, at the current time, apart from a few limited applications (eg, hematopoietic stem cell transplants for leukemia, epithelial stem cell-based transplants for burns, some treatments of corneal disease or injury), stem cells are not ready for routine clinical use. Indeed, while the promise is immense, a "large gap still exists between scientific knowledge and clinical translation for safe and effective stem cell-based therapies."³

*For the purpose of this discussion we distinguish stem cell tourism from other forms of medical tourism. In some cases patients travel to receive treatments or services that have been established to be safe and effective, for reasons related to wait times, cost, quality, or availability, among others. In other cases, the treatment sought might be highly controversial (eg, multiple sclerosis liberation). While some of the issues addressed in this paper might be relevant to other forms of medical tourism, the unique contextual factors relevant to those different forms merit focused consideration that is not within the scope of this commentary.

Despite this scientific reality, clinics around the world are leveraging the high profile of this exciting field and advertising unproven stem cell-based treatments for a range of conditions in a direct-to-consumer manner, usually via Internet marketing. There is no credible peer-reviewed evidence that the treatments offered by these clinics are safe or effective.⁴ They come at considerable financial cost, averaging around \$30 000 per treatment,⁵ often excluding the cost of travel and accommodation. Given the early state of stem cell science and the large amount of money involved in the stem cell tourism market, it seems safe to conclude that many of these clinics are knowingly exploiting vulnerable individuals by providing misleading or insufficient information about the efficacy (or lack thereof) and potential risks of the treatments offered. In some cases this conduct is likely fraudulent, in others reckless, and in others perhaps merely irresponsible. At the very least, until there is credible evidence of the safety and efficacy of these treatments, it remains a highly questionable and concerning practice.

It is unlikely that many Canadian physicians have had the opportunity to become equipped with sufficient knowledge of the stem cell tourism phenomenon to be able to offer their patients meaningful advice. In this brief commentary, we provide key points Canadian physicians can use to arm both themselves and their patients with the information necessary to make decisions that are as informed as possible. These points draw both on the existing literature on stem cell tourism and on emerging policy statements and patient resources (**Boxes 1 and 2**). It is not possible to address all potentially relevant topics in this forum. As is true in other areas, it is important that physicians act within the limits of their knowledge, skill, and judgment, which might mean acknowledging a lack of relevant expertise and working with patients to identify the appropriate experts and resources to consult. Ultimately, physicians who encounter the issue of stem cell tourism should strive to remain continually cognizant of their professional, legal, and ethical duties to their patients, particularly to minor patients and patients without decision-making capacity.

Key issues

There currently is no credible peer-reviewed evidence these treatments work. Research to date shows that

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Box 1. Helpful resources

The International Society for Stem Cell Research. *Patient Handbook on Stem Cell Therapies*
www.isscr.org/clinical_trans/pdfs/ISSCRPatientHandbook.pdf

The International Society for Stem Cell Research. *A Closer Look at Stem Cell Treatments*
www.closerlookatstemcells.org

Stem Cell Network website. (In particular, the "For the Public" section and FAQs)
www.stemcellnetwork.ca

Australian Stem Cell Centre. *Stem Cell Therapies: Now and in the Future*
www.msanz.org.nz/Document.Doc?id=23

United Kingdom National Stem Cell Network. *UKNSCN Position Statement on Stem Cell Tourism*
www.uknscn.org/downloads/stem_cell_tourism.pdf

Box 2. Other examples of guidance and information from patient groups and science organizations

ALSUntangled investigations (eg, "Update 4: Investigating the XCell-Center")
www.alsuntangled.com

Multiple Sclerosis Society, Sense About Science. *I've Got Nothing to Lose by Trying It*
www.senseaboutscience.org/data/files/resources/11/SAS002_NTL_HR.pdf

Parkinson Society Canada. *Stem Cell Research and Parkinson's Disease*
www.parkinson.ca/atf/cf/%7B9EBD08A9-7886-4B2D-A1C4-A131E7096BF8%7D/stem%20cells%20-%20en.pdf

Australia New Zealand Spinal Cord Injury Network. *Stem Cell Interventions for Spinal Cord Injury*
https://spinalnetwork.org.au/sites/default/files/file/E_StemCellBroch.pdf

Multiple Sclerosis Society. *Stem Cell Therapies in MS*
www.mssociety.org.uk/ms-resources/stem-cell-therapies

the claims made on provider websites are not supported by published peer-reviewed evidence of safety or efficacy, and in most cases lack credible scientific rationales, oversight, and transparency.⁴ (For an example, see the 2010 ALSUntangled Group study for their conclusions on an investigation of a particular clinic.⁶)

There are real risks involved. Virtually no medical treatment is without risk. Indeed, cell-based treatments in general are associated with a number of concerns, including rejection and infection. The use of stem cells introduces additional risks, largely because stem cell renewal and differentiation are so difficult to control. There is an enormous range of potential stem cell-based applications (eg, variation according to cell source and

type, genetic modification, autologous or allogenic use, homologous or nonhomologous use, method of administration), each associated with different types and degrees of risk. Contrary to the claims made on some websites, the fact that cells originally come from a person's body (eg, blood or bone marrow) does not mean they are safe to reintroduce after they have been manipulated outside the body. For example, cell characteristics can change during expansion, with the result that they lose the ability to differentiate into specialized cell types or to control their own growth. Cells might be subject to contamination with bacteria, viruses, or other pathogens. The jurisdiction in which the treatment is provided might have less than adequate infection control standards, thus heightening the contamination concern and creating other risks, such as the possibility of acquiring multiresistant pathogens. The fact that cell-based transplants might survive in a patient for many years and might in fact be irreversible makes the potential risks all the more salient. Already, and despite the absence of standardized reporting procedures, adverse events associated with unproven stem cell-based treatments have been noted, including tumours, meningitis, disability, and even death.⁷⁻¹⁰ Owing to the rapid evolution of this field, there are likely other currently unknown risks. Despite these concerns, it appears many clinics downplay the potential risks to prospective patients.

Patient testimonials and information on blogs should be viewed as unreliable. Anecdotal stories of success on websites and patient blogs are commonly used to promote medical tourism services. Patients considering these services should be exposed to the idea that testimonials are not evidence of a treatment's effectiveness. Factors including the placebo effect, fluctuating symptoms (particularly common in conditions like Parkinson disease and multiple sclerosis [MS]), and the possible effect of other treatments that commonly accompany the stem cell-based treatments considered here (eg, physiotherapy, acupuncture, massage, dietary changes) can encourage personal perceptions of benefit, particularly in the short term.

Media portrayals might lack balance. Popular representations (eg, newspaper stories) of stem cell research and its therapeutic potential can be overly optimistic, sometimes giving the impression that the research is closer to the clinic than it actually is. Research also shows that media reports of stem cell tourism tend to be very positive, focusing largely on the hopes of particular patients and their loved ones rather than on the associated risks and treatment uncertainties.¹¹ Such representations might create unrealistic expectations and misunderstandings among the public about the overall state of scientific and clinical consensus in the area of

stem cell research and translation, thereby lending legitimacy to clinics' claims.

The services should not be viewed as potentially beneficial experimental treatments. Although some providers now identify their treatments as "experimental," it does not mean that they operate in accordance with generally accepted standards for medical innovation outside of randomized clinical trials.¹² Further, paying to receive these unproven treatments is not the same thing as participating in a clinical trial. There are generally no preclinical data establishing safety and efficacy, nor any independent ethics review ensuring appropriate risk-benefit balance. Also, contrary to the beliefs expressed by some individuals, they will not be acting as "medical pioneers" if they receive unproven stem cell-based treatments overseas.¹³ Typically, these clinics do not publish their results or present their methods for peer review. Finally, it appears that prospective patients might not always be informed that receiving an unproven cell-based therapy will likely exclude them from participating in future clinical trials in their home jurisdictions.

It is highly unlikely that a single stem cell therapy will be developed that can cure or treat numerous diseases. Many clinics claim to treat an incredible variety of diseases and conditions with vastly different underlying causes (eg, autism to cancer, Alzheimer disease to MS, aging to amyotrophic lateral sclerosis) with the same therapy (including cell type and methods of administration). Such claims should constitute red flags for patients, as should clinics that have no or few limitations on eligibility to receive the treatment.

The stem cell tourism industry is driven by profit and enabled by evasion of oversight and accountability. As noted above, these treatments generally cost tens of thousands of dollars, and many individuals require help from family, friends, and community fundraisers to gather the necessary resources. While high costs might be a common feature of medical tourism and alone do not impugn the validity of the treatments, individuals should at minimum consider what will happen if they require emergency medical treatment overseas (ie, will it be covered by their insurance?). They should also be aware that the legal systems in many of the countries in which these treatments are offered do not allow medical negligence claims if something goes wrong.¹⁴

Working with patients and their caregivers

When discussing these issues with patients and their caregivers, it is essential that physicians be sensitive to the motivations underlying the interest in stem cell tourism. Research shows that many patients are motivated by desperation, the feeling that they have nothing to

lose, and a loss of faith in their own medical systems.¹³ The role hope plays in these decisions also cannot be underestimated,¹⁵ and the experiences that patient advocates bring to this issue suggest it is important that physicians be cognizant of the tone and form of their messaging. Even when individuals are dealing with a disease or condition for which treatments with good prospects are limited or simply nonexistent, there is great value in empowering them with knowledge about any ameliorative options that are available, including community and family supports. In addition to providing essential information, family physicians can be important partners in helping patients and their caregivers manage difficult diagnoses. Mere dismissal of stem cell tourism in the absence of other alternatives or supports is perhaps unlikely to resonate with individuals desperately searching for hope.

It is important to acknowledge that many individuals might not discuss these treatments with their family physicians, perhaps for fear of disapproval. Accordingly, physicians might wish to consider whether it is advisable to raise the issue prospectively in some cases, particularly when explaining diagnoses for diseases and disabilities that lack good treatment alternatives and which are often the focus of stem cell tourism marketing schemes (eg, autism, MS, amyotrophic lateral sclerosis, spinal cord injury, septooptic dysplasia). In other words, physicians could acknowledge to patients that people often do their own research on the Internet and come across these and other unproven treatments; if they do, they should know about some of the noted concerns.

Individuals determined to proceed with these unproven treatments should consider the value of obtaining information about key matters including what kinds of cells are being used, how they will be cultured and administered, whether they will be tested for disease and infection, and whether there are any follow-up procedures or protections in place in case of adverse reactions. Resources and other information that might be helpful are listed in **Boxes 1** and **2**. It is important to be aware that some clinics have responded to these guidance documents by preparing legitimate-sounding answers to the most common questions, but serious concerns nonetheless remain about the efficacy and safety of their treatments.

Conclusion

As stem cell research progresses and legitimate medical innovation using stem cell-based applications becomes more of a reality, the issues noted above are likely to become both more common and more complex. When the issue of stem cell tourism does arise, physicians are likely to struggle with how best to meet their professional, legal, and ethical obligations to their patients, including providing follow-up care for patients

who have received these treatments (perhaps even against the physician's advice). However, physicians are not alone in dealing with these issues. Indeed, as noted, there is a growing body of literature as well as scientifically informed policy statements to consult.

We in no way wish to place any blame or judgment on individuals who are determined to pursue hope in what are often extremely difficult and discouraging circumstances. The ultimate responsibility lies with the clinics and providers themselves. There are also various national-level responses emerging around the world, including attempts to develop and strengthen regulatory frameworks.¹⁶⁻¹⁸ While these efforts are commendable and vital, the challenges they encounter suggest a successful systemic response will be a long-term process. In the meantime, to respond to the risks individual Canadians are currently facing when entering this market, professionals working on the ground—including Canadian family physicians—have a critical role to play in ensuring that patients and their caregivers are making decisions that are as informed as possible and, especially when dealing with children and other individuals lacking decision-making capacity, truly in their best interests. 🍁

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None declared

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